Remarks

Reconsideration of this Application is respectfully requested.

Applicants thank the Examiner for the telephone interview of June 17, 2004. Applicants also thank the Examiner for the entry of claims 12 and 14-29 under 37 C.F.R. § 1.607. OA at page 11. Applicants also thank the Examiner for accepting the formal drawings and the removal of the objection regarding claim 5's compliance with the sequence rules.

The Office's statement that Applicant has presented an incomplete response under 37 C.F.R. § 1.607(a)(5) is addressed in detail below with respect to the written description rejection.

Upon entry of the foregoing amendment, claims 1, 2, 4-6, 8, 9, and 11-32 are pending in the application, with claims 1, 12, 14 and 21 being the independent claims. New claims 30-32 are sought to be added. Support for new claims 30-32 can be found throughout the specification and in the originally filed claims. These changes are believed to introduce no new matter, and their entry is respectfully requested. Claims 8, 9 and 11 have been amended to remove the multiple dependencies.

Entry of the amendments and the new claims will place the claims in condition for allowance or for better form for appeal. Accordingly, entry of the amendments and the new claims after final is believed proper and is respectfully requested.

Objections to the Claims

The objections to claims 2 and 13 as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim is respectfully traversed.

Without acquiescing to the objection, claim 1 has been amended to state that the vector for plant transformation comprises (i) a T-DNA sequence comprising a sequence located between two direct repeats and (ii) a gene encoding a toxin gene, a nucleotide sequence that interferes with DNA unwinding or an antisense housekeeping gene. Claim 2 now depends from claim 30, which is directed to the vector of claim 1, wherein the vector comprises a gene encoding a toxin gene. Claim 2 claims the vector according to claim 30, wherein the gene encoding a toxin gene is selected from the group consisting of an RNAse, a DNAse, a phytotoxin, a diphteria toxin, and a protease. Claim 13 now depends from claim 32, which is directed to a vector comprising an antisense housekeeping gene. Neither claim 2 nor claim 13 is broader in scope than the claims from which they depend. Accordingly, withdrawal of this objection is therefore respectfully requested.

Rejections under 35 U.S.C. § 112

Written Description Rejection

The rejection of claims 20 and 29 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement is respectfully traversed.

The claimed subject matter is described in the specification in such a way as to reasonably convey that the inventors, at the time the application was filed, had possession of the claimed invention. A skilled artisan, reading the disclosure at the time of the invention, would reasonably believe that the inventors had possession of a vector wherein the lethal polypeptide sequence is within about 5 kb of the left border. Both the working example inserting a Sal I site within the disclosed 5 kb, as well as the level of

skill in the art at the time of the invention, would clearly show that the inventors had possession of the claimed vector.

Support for the limitation "wherein the lethal polynucleotide sequence is within about 5 kb of the left border" is found, for example, at Example 1 at pp. 10-11. Specifically, Example 1 describes the construction of a binary vector backbone wherein a unique Sal I restriction endonuclease site was introduced into pMOG 800 so that elements aimed at inhibition of readthrough or counterselection of transgenics carrying vector sequences can be cloned next to the left border. The Sal I site is located 10 bp adjacent to the left border, which is within about 5 kb of the left border.

The rejection of claims 1, 4, 6 and 8-11 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement is respectfully traversed. Applicants thank the Examiner for the removal of this rejection regarding the term "a gene encoding a toxin gene."

The specification, at pages 8-9, teaches that read-through from the left border is inhibited by insertion of a nucleotide sequence outside the T-DNA border that interferes with the DNA unwinding process naturally needed for formation of a DNA molecule intended for translocation to the plant. Numerous examples of such a DNA sequence are disclosed in the specification. For example, the following types of sequences that interfere with the DNA unwinding process are detailed in the specification: (a) GC rich sequences, in particular, GC-rich sequences of approximately 20-60 basepairs, (b) sequences consisting of binding sites for *Agrobacterium* DNA-binding proteins, (c) sequences containing DNA-binding sites, and (c) the *vir* box. *See* specification at pages 8 and 9. Accordingly, one of skill in the art would recognize that as of the filing date the

inventors were in possession of a vector for plant transformation meeting the limitations of the claims.

The Office has also argued that the function of the genus of DNA sequences that interfere with DNA unwinding does not adequately describe the structure required to practice the claimed invention. Applicants respectfully disagree with the Office's reasoning. Specifically, the Office is using reasoning set forth in Federal Circuit cases, for example, *Reagents of the University of California v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997), that discuss written description of a claim directed to a *previously unknown DNA sequence.*

However, the claims present in the instant application are not analogous to the claims in *Lilly*. In *Lilly*, the patentee disclosed the sequence of a previously unknown nucleic acid sequence in a rat. The patentee then claimed all sequences that perform the same function as the rat sequence regardless of vertebrate species, e.g., in humans.

In contrast, claims of the instant invention are drawn to novel plant vectors that comprise a group of nucleotide sequences that interfere with DNA unwinding. Such sequences are well known in the art. As stated in the MPEP, "the use of known chemical compounds in a manner *auxiliary* to the invention must have a corresponding written description *only so specific as to lead one having ordinary skill in the art to that class of compounds*." *In re Hershchler*, 591 F.2d 693, 697, 200 USPQ 711, 714 (CCPA 1979), cited in MPEP § 2163 (emphasis added). The class of compounds, i.e., DNA sequences that interfere with DNA unwinding, are auxiliary to the claimed invention. That is, the present invention provides, *inter alia*, a vector comprising a T-DNA sequence where

read-through is prevented and sequences that interfere with DNA unwinding are one class of sequences that prevent read-through.

Accordingly, the above-identified portions of the specification provide a written description specific enough to lead one of ordinary skill in the art to a class of nucleotide sequences that interfere with DNA unwinding.

Claims 4, 6, 8 and 11 all depend, either directly or indirectly, from claim 1; for the reasons outlined above, each of these claims also has adequate written description.

Accordingly, withdrawal of this rejection is respectfully requested.

Enablement Rejection

The rejection of claims 1, 2, 4, 8, 9, 11 and 13 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement is respectfully traversed.

The test for enablement is "whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). One of reasonable skill in the art could make or use the presently claimed invention without undue experimentation.

The Office has argued that it would have required undue trial and error experimentation by one of skill in the art at the time the invention to make and use a vector for plant transformation comprising a nucleotide sequence that interferes with DNA unwinding as broadly claimed. Office Action at page 6-7. The Office argues that one of skill in the art would have been required to identify such nucleotide sequences, and introduce them into a vector for plant transformation at various locations to identify

those nucleic acid sequences and vector locations that would prevent incorporation of vector backbone sequences. Applicants respectfully disagree.

Contrary to the Offices' assertion that "one of skill in the art would have been required to ... introduce [nucleotide sequences that interfere with DNA unwinding] into a vector for plant transformation at various locations to identify those ... vector locations that would prevent incorporation of vector backbone sequences ..." the specification teaches sequences that interfere with DNA unwinding and their location on the vector. Specifically, the specification discloses that such sequences are located on the claimed vector close to the left T-DNA border. *See* specification at page 8. Moreover, the specification gives several examples of nucleotide sequences that will hamper the DNA unwinding process and their locations on the vector. For example, the specification identifies a sequence outside the T-DNA border that consists of binding sites for *Agrobacterium* DNA-binding proteins. The specification states "the presence of DNA-bound proteins *close to the left border* may physically interfere with assembly of the DNA-protein complex needed for unwinding of the DNA *downstream of the left border*." Specification at page 8 (emphasis added).

Moreover, the application contains specific examples that teach how to make vectors that incorporate DNA that interfere with the vector DNA unwinding. For example, Example 1 of the specification describes the creation of a binary vector backbone where "[a] unique Sal I restriction endonuclease site was introduced into pMOG 800 so that elements aimed at inhibition of readthrough or counterselection of transgenics carrying vector sequences, can be cloned next to the left border. *The site is located 10 bp adjacent to the left border*." Specification at page 10 (emphasis added).

The resulting plasmid is labeled pNE03. Example 2 describes the insertion of a 40 bp GC-rich stretch into the Sal I site. Such a 40 bp GC-rich stretch interferes with DNA unwinding. Likewise, Example 3 describes the insertion of virG binding sites into the vector which results in removal of the Sal I site at the side nearest the left T-DNA border. The Examples in the specification thus unmistakably teach how to make and use a vector comprising a nucleotide sequence that interferes with DNA unwinding.

Likewise, the specification teaches how to make and use a vector that comprises a sequence that is an antisense sequence for a housekeeping gene. The specification teaches that the sequences that prevent readthrough should be close to the left T-DNA border. Example 1 of the specification teaches creating a binary vector backbone where "[a] unique Sal I restriction endonuclease site was introduced into pMOG 800 so that elements aimed at inhibition of read through or counterselection of transgenics carrying vector sequences, can be cloned next to the left border. *The site is located 10 bp adjacent to the left border.*" Specification at page 10 (emphasis added). The resulting plasmid is labeled pNE03.

Insertion of a DNA sequence that is an antisense housekeeping sequence at the Sal I restriction site of the pNE03 would be well within the level of ordinary skill in the art. The specification describes in Examples 2-4 the insertion of various other sequences, including a GC-rich stretch, virG binding site and a barnase expression cassette. The specification thus provides adequate guidance for inserting an antisense housekeeping sequence into a vector comprising a T-DNA sequence.

For the reasons outlined above, each of these claims is adequately enabled.

Indefiniteness Rejection

The rejection of claims 1, 2, 4, 5, 6, 8, 9, 11 and 13 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is respectfully traversed.

The MPEP at section 2172 states that an indefiniteness rejection based on the failure to claim the subject matter that applicants regard as their invention "is appropriate only where applicant has stated, somewhere other than in the application as filed, that the invention is something different from what is defined by the claims . . . the invention set forth in the claims must be presumed, in the absence of evidence to the contrary, to be that which applicants regards as their invention." The Office has presented no evidence that Applicants have stated somewhere other than in the application that the invention is different than what is defined in the claims.

Applicants also respectfully disagree with the allegation that the metes and bounds of claim 1 are unclear. The Office states that the gene encoding a toxin or a nucleotide sequence that interferes with DNA unwinding must be located outside of the left T-DNA border, or else plant transformants would have more vector sequence than the T-DNA sequence. Claim 1 states that the sequence that prevents readthrough, i.e., the gene encoding a toxin gene, the nucleotide sequence that interferes with DNA unwinding or antisense housekeeping gene, is not located within the T-DNA sequence. The scope of the claim is clear and the public is informed of the boundaries of what constitutes infringement of the claim.

Claim 1 and its dependent claims 2, 4-6 and 8-11 are definite. Accordingly, withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. § 102

The rejection of claims 1, 2, 8, 11, 12 and 14-29 under 35 U.S.C. § 102(g) as anticipated by Gutterson *et al.*, U.S. Patent No. 6,521,458 ("Gutterson") is respectfully traversed.

Applicants reiterate that the Office has not established that Gutterson is prior art to the genus of compounds listed in the claims of the captioned application. The Office has also stated that the Applicant has only reduced to practice the same species as the prior art and has not provided evidence that they have reduced to practice any other species. Applicants respectfully disagree.

The specification indicates that several species encompassed by the genus of claim 1, for example, have been reduced to practice as of the filing date of the captioned application. For example, Examples 2 and 3 of the specification describe inserting two DNA sequences left of the border that interfere with DNA unwinding. Further, Example 1 of the specification describes the construction of a binary vector backbone that can be used to incorporate a variety of DNA sequences including, but not limited to, a variety of genes encoding toxin compounds. Further, the specification lists, for example at page 2, a variety of toxin compounds including, but not limited to RNAse, DNAse, phytotoxins, diphteria toxin and proteases. Such disclosure in the specification provides ample evidence that the inventors had possession of the genus as of the filing date.

Accordingly, withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. § 103

The rejection of claim 9 under 35 U.S.C. § 103 as allegedly unpatentable over U.S. Patent No. 6,521,458 is respectfully traversed. Claim 9 is drawn to a plant host comprising the vector according to claim 1, 2, 4, 5, or 6. As stated above, Gutterson (U.S. Patent No. 6,521,458) does not anticipate the claims of the present invention. Specifically, Gutterson does not disclose, teach or suggest the genus claimed in the present application. Withdrawal of this rejection is therefore respectfully requested.

The rejection of claims 1, 4, 5, 9 and 11 under 35 U.S.C. § 103 as allegedly being unpatentable over Ramanathan *et al.*, *Plant Molecular Biology 28*:1149-1154 (1995) ("Ramanathan") in view of D'Souza-Ault *et al.*, *J. Bacteriology 175*:3486-3490 (1993) ("D'Souza-Ault") is respectfully traversed.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, the prior art reference, or references when combined, must teach or suggest all the claim limitations. Second, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Last, there must be a reasonable expectation of success of practicing all of the claim limitations. MPEP § 2143.

Neither Ramanathan nor D'Souza-Ault, individually nor in combination, teach or suggest a vector for plant transformation comprising a T-DNA sequence, the T-DNA sequence comprising a sequence located between two direct repeats, and a gene encoding a toxin gene or a nucleotide sequence that interferes with DNA unwinding, or methods of using such a vector. Ramanathan teaches only that "it would be desirable to incorporate

into a [sic] T-DNA vectors a 'stop-transfer' signal adjacent to the left border." OA at page 10. Ramanathan does not state with any specificity whatsoever what such a "stop-transfer" signal would look like. Ramanathan does not teach or suggest any category of "stop-transfer" signal. The Office is using impermissible hindsight to state that the "stop-transfer" signal would inevitably be one of the nucleotides of the present invention, even though "stop-transfer" signal is such a vague and broad term as to encompass an enormous category of sequence.

D'Souza-Ault does not cure the deficiencies of Ramanathan. The Office states that

> D'Souza-Ault teaches a naturally occurring nucleotide sequence that would interfere with DNA unwinding, that being the Vir box and that *VirG acts as a repressor*. Given the general knowledge in the art at the time of the invention, one of ordinary skill in the art would have been motivated to use the Vir box sequence in a T-DNA construct adjacent to the left T-DNA border as suggested by Ramanathan to repress integration of vector sequence into a transformed plant.

OA at page 12 (emphasis added). Applicants respectfully disagree. D'Souza-Ault does not teach that the VirG sequence acts as a repressor of transcription. In fact, the opposite is true. It is the Ros box, the subject of D'Souza-Ault, that is the repressor. Specifically, D'Souza-Ault states that "[s]ome insight on how these latter operons are dually regulated is provided by the identification of the binding site for the Ros protein in the promoter region of *virC* and *virD*. The length of this binding site is 40 bp . . . This 40-bp sequence, termed the Ros box, overlaps the binding site (Vir box) of *the transcriptional activator VirG*." D'Souza-Ault at page 3489 (emphasis added). D'Souza-Ault further states that "VirG may modulate the expression of ros by serving as a repressor blocking

the transcription of ros when VirG is produced at high levels in induced *Agrobacterium* cells." *Id.* D'Souza-Ault thus teaches that VirG is an activator of transcription, and may repress the transcription of ros, which is a repressor.

In addition, nowhere does D'Souza-Ault teach or suggest that the Vir box is a "inhibitor of DNA unwinding." The claims of the instant application describe inserting a Vir box sequence outside of the T-DNA sequence and that such a sequence suppresses read-through beyond the T-DNA borders. Such suppression occurs because VirG is a binding protein that prevents the DNA outside the T-DNA border from unwinding.

Therefore, neither Ramanathan nor D'Souza-Ault, either individually or in combination, teach the claimed invention. There is also no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify either of the references or to combine the reference teachings. One of skill in the art would not be motivated to combine Ramanthan and D'Souza-Ault because, while Ramanathan suggests inserting a "stop-signal," the disclosure of D'Souza-Ault would not lead one of ordinary skill in the art to insert a Vir box. D'Souza-Ault does not teach that the Vir box sequence is a repressor of transcription, nor does D'Souza-Ault teach that such a sequence interferes with DNA unwinding.

Lastly, because the references, either alone or in combination, do not teach the claimed invention, there can be no reasonable expectation of success of practicing the combined teachings of the references to arrive at the claimed invention.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Date: March 1, 2005

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